REMARKS

The specification has been amended to delete references to certain web sites, and claim 1 has been amended to delete the recitation of "variants". No new matter is added by these amendments, and entry of the amendments is therefore requested.

The Examiner stated that claims 1-4 are currently under prosecution, claims 5-15 having been withdrawn from further consideration by the Examiner as drawn to non-elected inventions.

Objection to the Specification

The Examiner has objected to the specification because it contains an embedded hyperlink and/or other form of browser-executable code (i.e., see page 31, line 21). Applicant is required to delete all embedded hyperlinks and/or other form of browser-executable codes.

Applicants point out that the MPEP states at § 608.01 that this policy is based on the principle that "USPTO policy does not permit the USPTO to link to any commercial sites since the USPTO exercises no control over the organization, views or accuracy of the information contained on those outside sites (underline added). Section 608.01 goes on to state that "where hyperlinks and/or other forms of browser-executable codes are a part of the applicant's invention and it is necessary to have them included in the patent application in order to comply with the requirements of 35 U.S.C. 112, first paragraph, and applicant does not intend to have these hyperlinks as active links, examiners should not object to these hyperlinks. The Office will disable these hyperlinks when preparing the text to be loaded onto the USPTO web database (underline added). The web site recited at p. 30, line 10 is a non-commercial, government web site specifically associated with the National Center for Biotechnology Information (NCBI). In addition, Applicants further declare that this and the cited web site at page 31, line 21 were not intended as an active hyperlink but are recited in the interests of complying with 35 U.S.C. 112, first paragraph, and that their recitation in the application therefore complies with the requirements of the MPEP § 608.01. However, in the interests of expediting prosecution and the allowance of claims, the cited web sites have been deleted from the specification. Withdrawal of the objection is therefore requested.

35 U.S.C. § 101, Rejection of Claims 1-4

The Examiner has rejected claims 1-4 under 35 U.S.C. § 101, because the claimed invention is not supported by either a well-established or credible utility. The claims appear to

lack a well-established utility because of the following:

There appears to be conflicting examples regarding the amino acid of SEQ ID NO:4 encoded by the cDNA of SEQ ID NO:3. The specification clearly teaches that the amino acid sequence of SEQ ID NO:4 is a "tumor suppressor" protein (page 7, line 28). The conventional wisdom in the art regarding tumor suppressor genes is that loss of their expression or low amounts of expression (as compared to normal tissue) lead to uncontrolled proliferation (i.e. p53, rb). Indeed the specification teaches the results of microarray analysis comparing the differential expression of SEQ ID NO:4 in normal ovary tissue relative to ovary tumorous tissue. According to the specification, these results revealed a significant differential expression of SEQ ID NO:4 in ovary tumor and in treated ductal carcinoma cells and prostate cancer cells (page 12). Indeed, it appears that Applicants have shown that SEQ ID NO:4 is a tumor suppressor because the ratio of cancerous tissue to normal tissue expression provides negative values. However, regarding similar data from transcript imaging presented at pages 35-37 of the specification, the Examiner stated that, contrary to the microarray analysis data presented above, the relative abundance for the cDNA encoding SEQ ID NO:4 in all tumor tissues tested was a positive value compared to no expression in cytologically normal tissues. Thus, the Examiner stated, it appears that the cDNA encoding SEQ ID NO:4 has conflicting expression patterns and would lead on of ordinary skill in the art to question the credibility of the asserted utility regarding SEQ ID NO:4 as indeed a tumor suppressor. Thus, based on the information in the specification, the claimed polypeptide of SEQ ID NO:4 appears to lack a well-established and credible utility.

Applicants' Response

Applicants disagree that the disclosures of the specification are contradictory with respect to the identification of SEQ ID NO:4 as a tumor suppressor and that the specification therefore does not disclose either a well-established utility or a specific, substantial and credible asserted utility. On the contrary, applicants submit that a specific, substantial and credible utility is asserted by the specification, in particular in the use of the claimed polynucleotide in the detection and diagnosis of prostate cancer as stated at page 5, lines 4-6 of the specification, that is also consistent with the identification of SEQ ID NO:4 as a tumor suppressor. As the Examiner has correctly pointed out, the microarray data presented in the table at page 12 discloses a negative value for the differential expression (DE) of the polynucleotide encoding SEQ ID NO:4

in FGF treated prostate cancer cells relative to untreated cells. The DE values given in column 1 of the table are in fact expressed as the Log base 2 ($\log_2$) of the observed ratio, as it is conventional in the art. Thus, for the treated versus untreated prostate cancer cell line, DU145, the observed differential expression represents approximately a 2-fold lower expression in the untreated cells. While the microarray data for prostate tumor expression represents only a single observation, the Northern analysis data for prostate tissue expression represents multiple observations and is also consistent with the identification of SEQ ID NO:4 as a potential tumor suppressor. As disclosed in the specification at page 36, lines 17-19, summarizing the prostate tissue data, expression of the sequence encoding the tumor suppressor was seen as expected in early stage cancer (or precancerous conditions), such as benign prostate hyperplasia (BPH) or adenomatous hyperplasia (AH), or in cytologically normal tissues, which are matched with (m or mw) or associated with (aw) cancerous libraries, such as teratocarcinoma (TC), carcinoma (CA), or adenoCA in which expression was generally lower or undetectable. Thus, the presence of the transcript in prostate tissue is an indication of an early stage of prostate cancer or of normal tissue associated with cancerous prostate tissue in which expression of the transcript is less abundant or not expressed, i.e., "suppressed".

Moreover, the Office Action has ignored the fact that the recited polynucleotides and encoded polypeptides have specific, substantial, and credible utilities in, for example, toxicology testing in drug discovery, in particular, drug discovery related to the treatment of cancer, in particular, prostate cancer. One of skill in the art would know that, as a part of such toxicology testing, the recited polynucleotides and polypeptides could be used to detect toxic side effects of drug candidates targeted to a particular polypeptide in terms of their effects on the expression of other genes and their encoded polypeptides using any of a number of methods well known in the art for studying differential gene or protein expression, in particular, in a microarray format. See, for example, the specification, at p. 8, lines 14-20, and at p. 20, lines 25-32. Therefore, the claimed polypeptides meet the utility requirement of 35 U.S.C. § 101 based at least on the well-known, specific, and substantial utilities of expressed, naturally occurring polypeptides in toxicology testing and drug discovery.

Thus applicants submit that the specification supports a specific and substantial, credible utility for the the protein of SEQ ID NO:4 in the detection and diagnosis of prostate cancer,

particularly, earlier stage disease, and in toxicology testing and drug discovery, and therefore request withdrawal of the rejection of claims under 35 U.S.C. § 101.

35 U.S.C. § 112, First Paragraph, Rejection of Claims 1 and 4

The Examiner has rejected claims 1 and 4 under 35 U.S.C. § 112, first paragraph, as containing subject matter which is not described in the specification in such as way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner stated that the written description in this case only sets forth SEQ ID NO:4 and therefore the written description is not commensurate in scope with the claims drawn to naturally occurring amino acid sequences having at least 95% sequence identity to SEQ ID NO:4, which reads on variants of SEQ ID NO:4.

The Examiner then cited various court cases with respect to proper written description requirements, i.e., *Vas-Cath, Inc. v. Mahurkar* (applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed)*; *Fiers v. Revel* (Adequate written description requires more than mere statement that it is part of the invention and a reference to a potential method of making it); and *University of California v. Eli Lilly and Co.* (An adequate written description of a DNA...' requires a precise definition such as by structure, formula, chemical name, or physical properties' not a mere wish or plan for obtaining the claimed chemical invention).

Applicants' response

Applicants do not acquiesce to the Examiner's contention that the specification does not adequately define the claimed genus of variant polypeptides, particularly in structural terms. For example, the "variant language" of independent claim 1 recites chemical structure to define the claimed genus:

> 1. A purified protein comprising and amino acid sequences selected from the group consisting of:...b) an amino acid sequence having at least 95% sequence identity to the SEQ ID NO:4...

From the above it should be apparent that the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the

present claims is defined in terms of the chemical structure of SEQ ID NO:4. In the present case, there is no reliance merely on a description of functional characteristics of the polypeptides recited by the claims. In fact, there is no recitation of functional characteristics. Moreover, if such functional recitations were included, it would add to the structural characterization of the recited polypeptides. The polypeptides defined in the claims of the present application recite structural features, and cases such as *Lilly* and *Fiers* stress that the recitation of structure is an important factor to consider in a written description analysis of claims of this type.

However, in the interests of expiditing prosecution and the allowance of claims, variant language has been deleted from claim 1. Withdrawal of the rejection of claims 1 and 4 under 35 U.S.C. § 112, first paragraph is therefore requested.

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CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections/rejections. Early notice to that effect is earnestly solicited. Applicants further request that, upon allowance of claim 1, claims 5-8 be rejoined and examined as methods of use of the polypeptides of claim 1 that depend from and are of the same scope a claim 1 in accordance with *In re Ochiai* and the MPEP § 821.04.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at the number listed below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,
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